REMARKS

The present application was filed on March 27, 2001 (claiming priority from United States Provisional Application Number 60/245,396, filed November 2, 2000) with claims 1-43. Claims 7-21, 28-32 and 39-43 have been withdrawn from consideration in response to a restriction requirement and claims 4, 25 and 36 have been withdrawn from consideration in response to a species election. Therefore, claims 1-3, 5, 6, 22-24, 26, 27, 33-35, 37 and 38 are presented herein for examination on the merits. Applicant acknowledges that while claims 4, 7-21, 25, 28-32, 36 and 39-43 have been withdrawn from consideration, as highlighted above, these claims are still pending in the present application.

In the outstanding Office Action, the Examiner rejected claim 1, and claims dependent therefrom, under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. The Examiner further rejected claims 1-3, 5, 6, 22-24, 26, 27, 33-35, 37 and 38 under 35 U.S.C. §101 because the claimed invention allegedly lacks patentable utility. The Examiner rejected claims 1, 3, 6, 22, 24, 27, 33, 35 and 38 under 35 U.S.C. §102(b) as allegedly anticipated by J. L. Cornette et al., *Hydrophobicity Scales and Computational Techniques for Detecting Amphipathic Structures in Proteins*, J. MOL. BIOL. 195, pgs. 659-685 (1987) (hereinafter "Cornette"). The Examiner further rejected claims 1-3, 6, 22, 24, 27, 33, 35 and 38 under 35 U.S.C. §102(b) as allegedly anticipated by Eisenberg et al. Faraday Symposia of the Chemical Society, 1982, 17, 109-120 (hereinafter "Eisenberg"). The Examiner also objected to the specification as containing an embedded hyperlink and/or other form of browser-executable code.

The present invention has been described in Applicant's prior response, incorporated by reference herein.

FORMAL REJECTIONS

As mentioned above, the Examiner rejected claim 1, and claims dependent therefrom, under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. Specifically, the

Examiner stated, with regard to independent claim 1, that the claim is "indefinite due to the lack of clarity of the claim language failing to recite a final process step, which agrees back with the preamble." See, Office Action, beginning on page 2, 3rd paragraph. Specifically, the Examiner stated that the "claim does not set forth the conditions when determining/shifting of hydrophobicity distribution results in 'spatially profiling proteins.'" See *Id.* Applicants respectfully disagree with the Examiner's assertions.

Applicants submit that the steps of determining a hydrophobicity distribution for a protein and shifting the hydrophobicity distribution, as recited in independent claim 1, "agree[] back with the preamble" of that claim, as these are steps performed in spatially profiling a protein. By way of example only, Applicants point to page 4, line 26, to page 5, line 1, of the specification wherein it is explained that the "hydrophobicity distribution can be shifted and normalized, which places each protein with mathematical basis for comparison." Thus, the shifted hydrophobicity distribution of a protein, as in independent claim 1, is associated with the spatial profile of the protein.

Furthermore, Applicants point to page 9, lines 15-19, of the specification wherein it is stated that,

> [s]uch shifting of the values of amino acid hydrophobicity eliminates the zero-order moment from the distribution and, consequently, the dependence of the second-order moment upon differences in net protein hydrophobicity. This provides a basis for comparison of the hydrophobic moment profiles of the different proteins and, consequently, a basis for comparison of their hydrophobic rations.

Given the above remarks, Applicant respectfully asserts that claim 1 does "set forth the conditions when determining/shifting of hydrophobicity distribution results in 'spatially profiling proteins." Consequently, it is Applicant's position that one of ordinary skill in the art would be able to ascertain the metes and bounds of the present claims from the teachings of the specification. Thus, Applicant respectfully requests reconsideration and withdrawal of the rejection.

As further highlighted above, the Examiner rejected claims 1-3, 5, 6, 22-24, 26, 27, 33-35, 37 and 38 under 35 U.S.C. §101 because the claimed invention allegedly lacks

patentable utility. Specifically, the Examiner stated beginning on page 3, 4th paragraph of the Office Action that,

> [t]he claims are directed to a method of shifting hydrophobicity distribution of a protein. The claims do not recite any particular result of such "shifting" or "spatial profiling" and do not recite any particular protein of interest for which such analysis would yield any identified useful information.

Applicant respectfully disagrees with the Examiner's assertions. First, as Applicant previously pointed out, independent claim 1, from which claims 2, 3, 5 and 6 ultimately depend, is expressly directed to a practical method for "spatially profiling proteins." Thus, these claims are clearly tied to a practical application. A process that is limited to a practical application of an abstract idea or mathematical algorithm in the technological arts is patentable. See Examination Guidelines for Computer-Related Inventions, § IV. B. 2. b. (ii). In any event, the analysis does not stop there. The Supreme Court has stated that the "[t]ransformation and reduction of an article 'to a different state or thing' is the clue to patentability of a process claim." Gottshalk v. Benson, 409 U.S. 63, 70, 175 U.S.P.Q. (BNA) 676 (1972). In other words, claims that require some kind of transformation of subject matter, which has been held to include intangible subject matter, such as data or signals, that are representative of or constitute physical activity or objects have been held to comply with § 101. See, for example, In re Warmerdam, 31 U.S.P.Q.2d (BNA) 1754, 1759 n.5 (Fed. Cir. 1994) or In re Schrader, 22 F.3d 290, 295, 30 U.S.P.Q.2d (BNA) 1455, 1459 n.12 (Fed. Cir. 1994). Applicant, by way of example only, points to page 4, line 27, through page 5, line 9, where it is stated that,

> [t]he resultant hydrophobicity distribution can be shifted and normalized, which places each protein with mathematical basis for comparison. Without shifting the hydrophobicity distribution, the ability to compare different proteins is significantly degraded.... After shifting and/or normalizing the hydrophobicity distribution, the adjusted zero- and second-order moments of the hydrophobicity distribution can be determined.... The shape or profile of the adjusted second-order moment can be used to determine if a protein is globular.

Furthermore, as set forth, for example, beginning on page 5, line 15, of the specification, it is provided that, e.g., globular proteins can be distinguished from other proteins or decoys by determining a ratio of the distance at which the adjusted second-order moment of

hydrophobicity vanishes and the distance at which the adjusted zero-order moment of hydrophobicity vanishes (or vice versa).

Additionally, one skilled in the art would affirm that there are a great number of 1-D amino acid sequences but only a limited number of 3-D protein structures, and therefore there is an outstanding problem of converting the 1-dimensional amino acid sequences into the protein three-dimensional structures that are essential for providing the information required for better understanding biological processes. See, for example, page 2, lines 1-13, of the specification. Therefore, the claimed invention encompasses much more than basic research and Applicants respectfully assert that the claimed invention has significant practical utility in the "real world" because it provides a quick, single measure that substantiates predicted 3-dimensional protein structure inferred from one-dimensional sequence data.

Given the above remarks, Applicant respectfully submits that claims 1-3, 5, 6, 22-24, 26, 27, 33-35, 37 and 38 fully comport with the requirements of 35 U.S.C. §101 and as such, Applicant respectfully requests reconsideration and withdrawal of the rejections.

As mentioned above, the Examiner also objected to the specification as containing an embedded hyperlink and/or other form of browser-executable code. Applicant has amended to the specification at page 17, lines 7-8, to remove the web site address appearing therein. The same amendment was included in the previous Office Action Response, dated July 18, 2005, but the Examiner has made no mention to it in this Office Action. Reconsideration and withdrawal of the rejection is thus respectfully requested.

PRIOR ART REJECTIONS

As mentioned above, the Examiner rejected claims 1, 3, 6, 22, 24, 27, 33, 35 and 38 under 35 U.S.C. §102(b) as allegedly unpatentable over Cornette. On page 5, 5th paragraph, of the Office Action, the Examiner stated that,

> Cornette teaches calculation of hydrophobic moment for each residue (cf. claim 6) - i.e., determining 'hydrophobicity distribution' - and plotting them on a graph. See p. 660, right column through p. 661, left column, and Fig. 2.... For comparative purposes, to compare different approaches, the

hydrophobicity values are normalized (cf. claim 3) to have a value of 1000 at the frequency angle of 100° (i.e., 'hydrophobicity distribution' is 'shifted').

Applicant has amended independent claim 1, thereby overcoming the Examiner's rejections. Support for the amendment can be found, for example, on page 1, lines 14-18, and page 8, lines 1-4 of the specification. Applicant argues that Cornette focuses exclusively on secondary structure, i.e., alpha helices. See, for example, page 660, left column. Applicant asserts, however, that the presently claimed invention teaches shifting of the hydrophobicity distribution that had never been previously performed in connection with three-dimensional structure. For example, Applicant points to page 1, lines 14-16, of the specification, where it is stated that,

> [w]hen profiling a protein, researchers attempt to determine the order of the colors of the beads and where the beads are in three-dimensional space. (emphasis added).

Further, Applicants point to page 8, lines 1-4, of the specification, where it is stated that,

> [t]his could provide useful information with respect to the three-dimensional spatial affinity of the tertiary protein structure and external structures with which it might interact. Thus, these equations provide insight into protein structures. (emphasis added).

Cornette, however, does not teach a method for determining three-dimensional protein structure, but rather focuses exclusively on secondary structure segments, i.e. alpha-helices. For example, Applicant points to page 659, first paragraph, of the Cornette reference, where it is stated that,

> Protein segments that form amphipathic α-helices in their native state have periodic variation in the hydrophobicity values of the residues along the segment, with a 3.6 residue per cycle period characteristic of the α-helix.... Thirty-eight published hydrophobicity scales are compared for their ability to identify the characteristic period of α-helices, and an optimum scale for this purpose is computed using a new eigenvector method. (emphasis added).

Further, on page 659, fourth paragraph, of the Cornette reference, it is stated that,

> [a]lthough the scale is optimal only for predicting α-amphipathicity, it also ranks high in identifying β-amphipathicity.... (emphasis added).

Therefore, Applicant submits that because Cornette focuses exclusively on secondary structure, claims 1, 3, 6, 22, 24, 27, 33, 35 and 38 of the present invention are not anticipated by Cornette. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The amended independent claim 1 contains an element - a method to describe three-dimensional structure of a protein - that is not found in the Cornette reference.

As such, Applicants respectfully requests reconsideration and withdrawal of the rejection of claims 1, 3, 6, 22, 24, 27, 33, 35 and 38 over Cornette.

As mentioned above, the Examiner also rejected claims 1-3, 6, 22, 24, 27, 33, 35 and 38 under 35 U.S.C. §102(b) as allegedly anticipated by Eisenberg. On page 6, 6th paragraph, of the Office Action, the Examiner stated that,

> Eisenberg et al describes determination of hydrophobicity distribution in proteins. To reconcile 'hydrophobicity scales' from different publications which provide values of hydrophobicity for amino acid residues, Eisenberg 'normalized' hydrophobicity. The scales were combined by averaging the normalized hydrophobicities for each residue over five scales, the result was multiplied by standart deviation and added to its mean. See p. 110 and Table 1. Therefore, the Eisenberg reference reads on the instantly claimed method comprising steps of shifting hydrophobicity distribution based on a difference between values in the hydrophobicity distribution and an average hydrophobicity value.

Applicant respectfully traverses the Examiner's rejections. Applicant points to page 4, line 24, through page 5, line 2, of the specification, where it is stated that,

> [a] hydrophobicity scale can be used to determine the hydrophobicity distribution of a protein.... The resultant hydrophobicity distribution can be shifted and normalized, which places each protein with mathematical basis for comparison. Without shifting the hydrophobicity distribution, the ability to compare different proteins is significantly degraded. (Emphasis added).

Further, Applicant points to page 9, lines 4-8, wherein it is stated that,

> [t]he hydrophobicity distribution arises from the spatial distribution of residues and their assigned values of hydrophobicity. The distribution of amino acid hydrophobicity is, however, shifted (step 140) such that the net hydrophobicity of each protein vanishes. This is done by subtracting the average hydrophobicity from each value in the hydrophobicity distribution. (Emphasis added).

The material in the Eisenberg reference noted by the Examiner - p. 110 and Table 1 - in the outstanding Action is only directed to the means by which the "consensus" hydrophobicity scale was created, and does not teach the step of subsequently shifting the hydrophobicity distribution. Applicant points to page 110, third paragraph, of the Eisenberg reference, wherein it is stated that,

> [t]he consensus scale was derived as follows. We noted that for each of the four complete hydrophobicity scales on the left of table 1, the value for serine lies at the mean, or very close to it. For each scale, the standard deviation of the hydrophobicities was determined. The "normalized" hydrophobicity of a residue in each scale was defined as the number of standard deviations that its hydrophobicity lay above or below the mean. The scales were combined by averaging the normalized hydrophobicities for each residue over the five scales.

As noted by Applicant above, a hydrophobicity scale can be used to determine the hydrophobicity distribution of a protein. Eisenberg teaches the creation of one hydrophobicity scale. However, Eisenberg does not teach the subsequent shifting of the hydrophobicity distribution based on a difference between values in the hydrophobicity distribution and an average hydrophobicity value.

Therefore, Applicant submits that the step of "shifting the hydrophobicity distribution" as stated in independent claim 1 of the present invention is not anticipated by Eisenberg.

As such, Applicants respectfully requests reconsideration and withdrawal of the rejection of claims 1, 3, 6, 22, 24, 27, 33, 35 and 38 over Eisenberg.

In view of the foregoing, the invention cannot be said to be taught or suggested by Cornette or Eisenberg. Accordingly, Applicant submits that all claims presented here for examination, i.e., claims 1-3, 5, 6, 22-24, 26, 27, 33-35, 37 and 38, are in condition for allowance and such favorable action is earnestly solicited.

If any outstanding issues remain, or if the Examiner has any further suggestions for expediting allowance of this application, the Examiner is invited to contact the undersigned at the telephone number indicated below.

The Examiner's attention to this matter is appreciated.

Respectfully submitted,

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